Understanding Stem Cells and their Potential Applications

Abstract

Stem cells possess a unique property in that they are able to differentiate into a panoply of cells present in living organisms, both in initial developmental and subsequent regenerative roles. The sequential mechanism involved in this process presents an opportunity to increase our understanding of cell lineages, and consequently apply this understanding to exploring new avenues of medical treatment and research. Applications explored include leukemia, breast cancer, diabetes and neural regeneration, although numerous other potential areas have been identified, and make for an exciting time ahead.

Introduction

The term "stem cell" was at first used by Russian histologist Alexander Maksimov in 1908 in postulation of the existence of hematopoietic stem cells. Amazing strides have been made since then in our understanding of how these biological cells can differentiate into diverse specialized cell types. Stem cells can be divided into two main broad types: **embryonic stem cells** in blastocysts, and **adult stem cells** that can be found in a wide variety of tissues. In the former case, they are responsible for the eventual formation of all differentiated cell types in the organism through successive cell lineages. In the latter case, they constitute a repair system for the repeated renewal of cells. The potential applications of stem cell therapy are extremely lucrative, prompting extensive research with respect to diseases including cancer, multiple sclerosis, Parkinson's disease, Amyotrophic lateral sclerosis and even spinal cord injuries.[iii] Study of stem cell differentiation mechanisms, in addition to being academically fascinating, is therefore also an extremely lucrative avenue of clinical treatment research.

Understanding the Stem Cell Paradigm

Stem cell differentiation involves a marvelous multistage process, in which the initial totipotent stem cell progressively loses differentiation capability as it progresses along a certain lineage. This can be illustrated below:

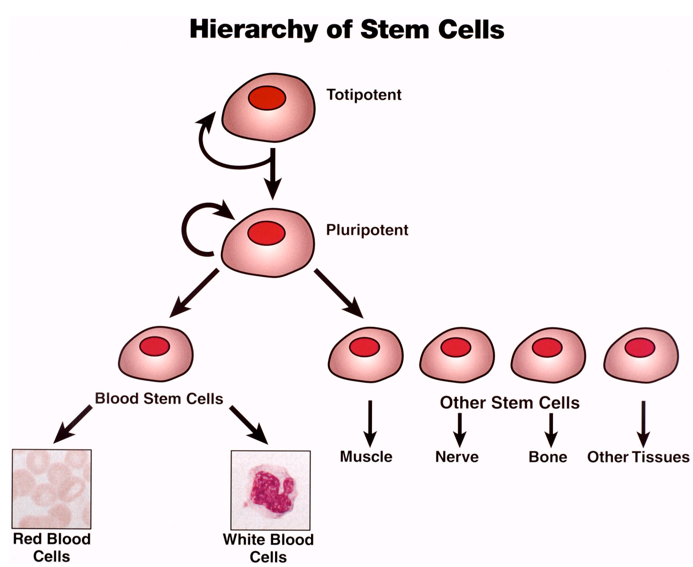

Figure 1[iii]

Figure 1 shows the various stages of differentiation. Let us examine this in more detail so that we can later expound upon the implications to leukemia, breast cancer and other maladies. The stem cell, of which there are both long-term and short-term instances, initially differentiate into **multipotent progenitors**. These have full lineage potential.[iv] However these subsequently divide into **oligopotent progenitors** that have only a few potential lineages, for example within muscle or nerve cells. At that point, they commit to a single lineage.

Application to our Understanding of Leukemia Stem Cell Hierarchy

One of the most interesting applications of stem cell research mentioned in Dr. Weissman's lecture was the application to the analysis of cancers such as Leukemia.

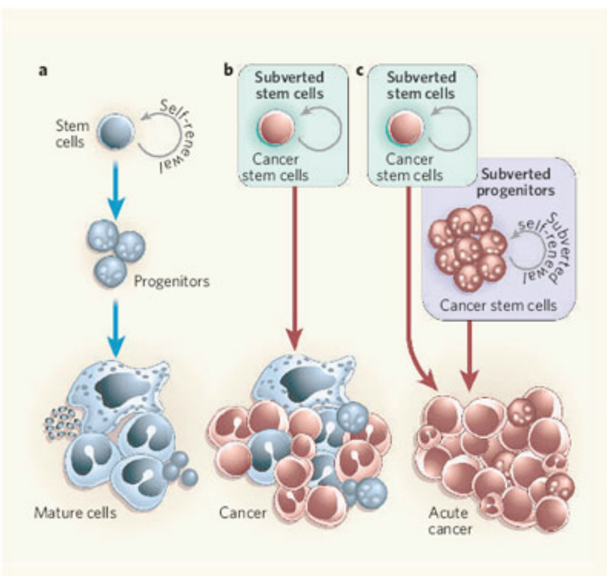

Figure 2 [v]

Our understanding of the stem cell paradigm allows us to postulate, and subsequently verify, the idea that a cancer may develop due to unregulated stem cell renewal, as illustrated in Figure 2 above. We see that **a** represents normal stem cell self-renewal and differentiation. Part **b** illustrates unregulated stem cell self-renewal, while **c** shows subverted progenitors as well.

The following Figure 3 demonstrates the potency of an example application of the resultant understanding of the cancer mechanism.

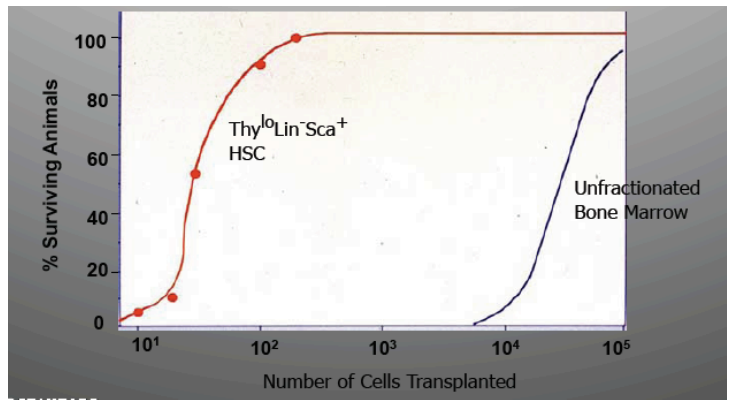

Figure 3[iv]

Spangrude, Heimfield and Weissman have found in mice that purified stem cell populations with a Sca 1+ Lin- Thy 1- surface phenotype constitute a 50-100% pure population of spleen colony-forming cells. In Figure 3, we see that a much lower number of cells need be transplanted for similar survival rates, as compared to unfractionated bone marrow: this approach is effectively 2000 more effective in radioprotection and restoring blood formation.[vi]

Let us now explore how similar approaches can be taken in the treatment of breast cancer.

Application to Breast Cancer

Consider applying this to the treatment of breast cancer. In the hematopoietic stem cell (HSC) case, there are two mechanisms to purification:

1. Self-Donor Transplant;
2. Healthy Donor Transplant.

These are illustrated in figures 4 and 5 respectively.

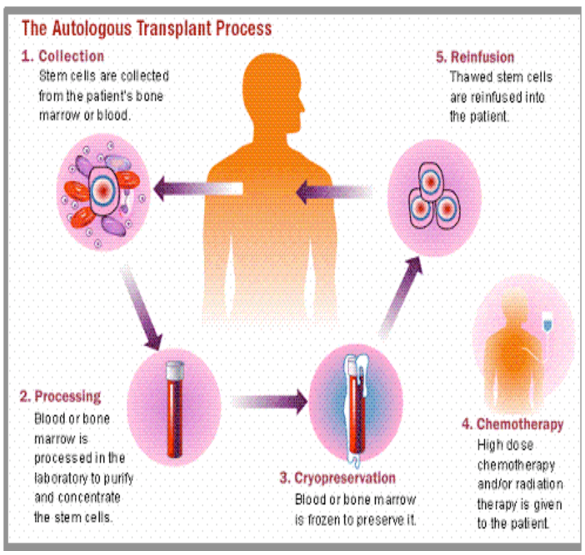

Figure 4 - Here cells of the patient are purified, then reinserted. [vii]

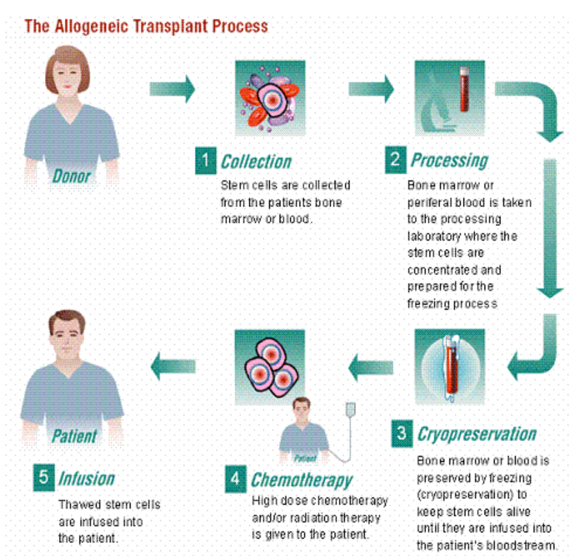

Figure 5 - In this case, the recipient undergoes radiation damage or therapy, and is given healthy donor cells. [viii]

The results can be astounding. A study by Negrin et al, referenced by Dr. Weissman in his lecture demonstrates superior survival rates among breast cancer patients after HSC transplant, as evinced in Figure 6:

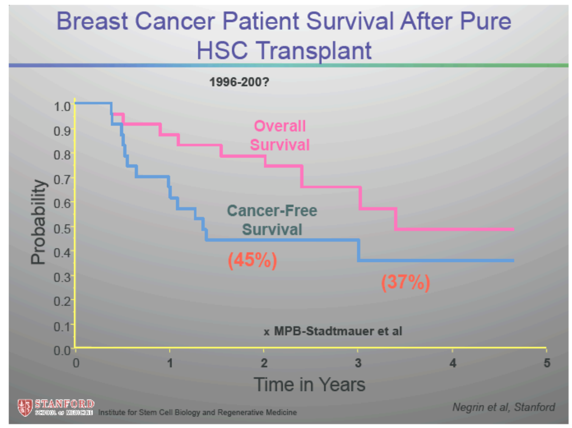

Figure 6 [iv]

Unfortunately, it would appear such a therapy was not immediately pursued due to limited commercial profitability – despite resounding clinical efficacy. This capitalist characteristic of clinical therapy development, in large part due to the high costs associated, is noteworthy.

That said, the applications of stem cell transplantation and purification are not limited to cancer treatment, as we shall now explore.

Other Applications: an Illustration

Potentially more commercial applications of stem cell transplantation could include diseases like **diabetes mellitus**. Diabetes affects 18 million people in the U.S. alone (8.7% of the population) and more than 190 million worldwide.[ix] As Dr. Weissman argues, contrary to what some believe, "diabetes is a stem cell disease". [iv]

Shapiro et al have demonstrated that islet transplantation in patients with type 1 diabetes can lead to a drastic reduction in circadian blood glucose concentration fluctuations.[x]

Another possible treatment suggested that uses stem cells, for illustrative purposes, could be for **brain damage** or brain degeneration such as **Parkinson's** and **Alzheimer's diseases.**[xi] [xii]

In fact, applications have even been extended to areas such as **spinal cord recovery**. Korean researchers in 2003 injected adult stem cells into a patient's damaged spinal cord, achieving tangible improvement in mobility.[xiii] More recently, in 2005 University of California, Irvine researchers similarly achieved transplanted stem cell differentiation in paralyzed mice, resulting in significant locomotor improvement.[xiv]

Other measurements of improvement using stem cell treatment include the direct detection of electrical signals of newly developed motor neurons. Researchers at the University of Wisconsin-Madison have done so with blastocysts stem cells converted into neural stem cells in 2005.[xv]

Closing Remarks and Future Direction

Although the term "stem cell" may have been coined over a century ago, it is safe to say that the field is still in its infancy. Although a general paradigm of stem cell differentiation has been laid out, and specificities continue to be explored, there is still a wealth of intricacies in the particular mechanisms at play going from a totipotent cell to a single committed lineage.

What is arguably even more appealing is the fact that applications of the theory are also only incipient. The myriad of possible treatments offered by stem cell therapy, of which leukemia, breast cancer, diabetes and neural regeneration are only a few examples, ensures the next decades and beyond of stem cell research will both be critical and extremely interesting.

Further exploration into the theoretical mechanisms, the practical applications, and as observed the commercial feasibility of stem cell treatment will hopefully result in a more solid realization of the potential of this astounding field.

References

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